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General information about the entry

Entry name	CCR4_HUMAN
Primary accession number	P30991
Secondary accession numbers	O60835 P56438 Q9UKN2
Entered in Swiss-Prot in	Release 26, July 1993
Sequence was last modified in	Release 26, July 1993
Annotations were last modified in	Release 41, February 2003

Name and origin of the protein

Protein name	C-X-C chemokine receptor type 4
Synonyms	CXC-R4 CXCR-4 Stromal cell-derived factor 1 receptor SDF-1 receptor Fusin Leukocyte-derived seven transmembrane domain receptor LESTR LCR1 FB22 NPYRL HM89 CD184 antigen
Gene name	CXCR4

From	Homo sapiens (Human) [TaxID: 9606] Pan troglodytes (Chimpanzee) [TaxID: 9598]
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Taxonomy	Eukaryota ; Metazoa ; Chordata ; Craniata ; Vertebrata ; Euteleostomi ; Mammalia ; Eutheria ; Primates ; Catarrhini ; Hominidae ; Homo .
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References

- [1] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).
SPECIES=Human;
TISSUE=Lung;
MEDLINE=93319629; PubMed=8329116; [NCBI, ExPASy, EBI, Israel, Japan]
[Herzog H.](#), [Hort Y.J.](#), [Shine J.](#), [Selbie L.A.](#);
"Molecular cloning, characterization, and localization of the human homolog to the reported bovine NPY Y3 receptor: lack of NPY binding and activation.";
DNA Cell Biol. 12:465-471(1993).
- [2] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).
SPECIES=Human;
TISSUE=Fetal brain;
MEDLINE=94052833; PubMed=8234909; [NCBI, ExPASy, EBI, Israel, Japan]
[Jazin E.E.](#), [Yoo H.](#), [Blomqvist A.G.](#), [Yee F.](#), [Weng G.](#), [Walker M.W.](#), [Salon J.](#), [Larhammar D.](#), [Wahlestedt C.R.](#);
"A proposed bovine neuropeptide Y (NPY) receptor cDNA clone, or its human homologue, confers neither NPY binding sites nor NPY responsiveness on transfected cells.";

Regul. Pept. 47:247-258(1993).

[3] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

SPECIES=Human;

TISSUE=Fetal spleen;

MEDLINE=93315164; PubMed=8325644; [NCBI, ExPASy, EBI, Israel, Japan]

Federspiel B., Melhado I.G., Duncan A.M., Delaney A.D., Schappert K.T., Clark-Lewis I., Jirik F.R.;

"Molecular cloning of the cDNA and chromosomal localization of the gene for a putative seven-transmembrane segment (7-TMS) receptor isolated from human spleen.";

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[4] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

SPECIES=Human;

TISSUE=Monocytes;

MEDLINE=94103215; PubMed=8276799; [NCBI, ExPASy, EBI, Israel, Japan]

Loetscher M., Geiser T., O'Reilly T., Zwahlen R., Baggiolini M., Moser B.;

"Cloning of a human seven-transmembrane domain receptor, LESTR, that is highly expressed in leukocytes.";

J. Biol. Chem. 269:232-237(1994).

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SPECIES=Human;

TISSUE=Monocytes;

MEDLINE=94092629; PubMed=7505609; [NCBI, ExPASy, EBI, Israel, Japan]

Nomura H., Nielsen B.W., Matsushima K.;

"Molecular cloning of cDNAs encoding a LD78 receptor and putative leukocyte chemotactic peptide receptors.";

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[6] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1), AND CHARACTERIZATION OF ITS HIV-1 CORECEPTOR FUNCTION.

MEDLINE=96217947; PubMed=8629022; [NCBI, ExPASy, EBI, Israel, Japan]

Feng Y., Broder C.C., Kennedy P.E., Berger E.A.;

"HIV-1 cofactor: functional cDNA cloning of a seven-transmembrane, G protein-coupled receptor.";

Science 272:872-877(1996).

[7] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

SPECIES=Human;

TISSUE=Peripheral blood leukocytes;

MEDLINE=98136183; PubMed=9468539; [NCBI, ExPASy, EBI, Israel, Japan]

Wegner S.A., Ehrenberg P.K., Chang G., Dayhoff D.E., Sleeker A.L., Michael N.L.;

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J. Biol. Chem. 273:4754-4760(1998).

[8] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

SPECIES=Human;

MEDLINE=98258970; PubMed=9599023; [NCBI, ExPASy, EBI, Israel, Japan]

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[9] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

SPECIES=Human;

MEDLINE=99408510; PubMed=10480633; [NCBI, ExPASy, EBI, Israel, Japan]

Xiao L., Weiss S.H., Qari S.H., Rudolph D., Zhao C., Denny T.N., Hodge T., Lal R.B.;

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[10] SEQUENCE FROM NUCLEIC ACID (ISOFORM 1).

SPECIES=Human;

TISSUE=Peripheral blood lymphocytes;

MEDLINE=99095114; PubMed=9879064; [NCBI, ExPASy, EBI, Israel, Japan]

Frodl R., Gierschik P., Moepps B.;

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J. Recept. Signal Transduct. Res. 18:321-344(1998).

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SPECIES=Human;

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MEDLINE=99384048; PubMed=10452968; [NCBI, ExPASy, EBI, Israel, Japan]

Gupta S.K., Pillarisetti K.;

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SPECIES=P.troglodytes;

MEDLINE=98090115; PubMed=9430250; [NCBI, ExPASy, EBI, Israel, Japan]

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[13] SULFATION.

SPECIES=Human;

MEDLINE=99189752; PubMed=10089882; [NCBI, ExPASy, EBI, Israel, Japan]

Farzan M., Mirzabekov T., Kolchinsky P., Wyatt R., Cayabyab M., Gerard N.P., Gerard C., Sodroski J., Choe H.;

"Tyrosine sulfation of the amino terminus of CCR5 facilitates HIV-1 entry.";
Cell 96:667-676(1999).

[14] FUNCTION.

MEDLINE=96351077; PubMed=8752280; [NCBI, ExPASy, EBI, Israel, Japan]

Bleul C.C., Farzan M., Choe H., Parolin C., Clark-Lewis I., Sodroski J., Springer T.A.;

"The lymphocyte chemoattractant SDF-1 is a ligand for LESTR/fusin and blocks HIV-1 entry.";
Nature 382:829-833(1996).

[15] FUNCTION.

MEDLINE=96351078; PubMed=8752281; [NCBI, ExPASy, EBI, Israel, Japan]

Oberlin E., Amara A., Bachelier F., Bessia C., Virelizier J.-L., Arenzana-Seisdedos F., Schwartz O., Heard J.-M., Clark-Lewis I., Legler D.F., Loetscher M., Baggiolini M., Moser B.;

"The CXCR chemokine SDF-1 is the ligand for LESTR/fusin and prevents infection by T-cell-line-adapted HIV-1.";
Nature 382:833-835(1996).

[16] ERRATUM.

Oberlin E., Amara A., Bachelier F., Bessia C., Virelizier J.-L., Arenzana-Seisdedos F., Schwartz O., Heard J.-M., Clark-Lewis I., Legler D.F., Loetscher M., Baggiolini M., Moser B.;

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[17] CHARACTERIZATION OF ITS HIV-1 CORECEPTOR FUNCTION.

MEDLINE=97002453; PubMed=8849450; [NCBI, ExPASy, EBI, Israel, Japan]

Lapham C.K., Ouyang J., Chandrasekhar B., Nguyen N.Y., Dimitrov D.S., Golding H.;

"Evidence for cell-surface association between fusin and the CD4-gp120 complex in human cell lines.";
Science 274:602-605(1996).

[18] CHARACTERIZATION OF ITS HIV-2 RECEPTOR FUNCTION.

MEDLINE=97083584; PubMed=8929542; [NCBI, ExPASy, EBI, Israel, Japan]

Endres M.J., Clapham P.R., Marsh M., Ahuja M., Turner J.D., McKnight A., Thomas J.F., Stoeckenau-Haggarty B.;

Choe S., Vance P.J., Wells T.N.C., Power C.A., Sutterwala S.S., Doms R.W., Landau N.R., Hoxie J.A.;

"CD4-independent infection by HIV-2 is mediated by fusin/CXCR4.";
Cell 87:745-756(1996).

Comments

- **FUNCTION:** RECEPTOR FOR THE C-X-C CHEMOKINE SDF-1. TRANSDUCES A SIGNAL BY INCREASING THE INTRACELLULAR CALCIUM IONS LEVEL. INVOLVED IN HAEMATOPOIESIS AND IN CARDIAC VENTRICULAR SEPTUM FORMATION. PLAYS ALSO AN ESSENTIAL ROLE IN VASCULARIZATION OF THE GASTROINTESTINAL TRACT, PROBABLY BY REGULATING VASCULAR BRANCHING AND/OR REMODELLING PROCESSES IN ENDOTHELIAL CELLS. COULD BE INVOLVED IN CEREBELLAR DEVELOPMENT. IN THE CNS, COULD MEDIATE HIPPOCAMPAL-NEURON SURVIVAL. ACTS AS A PRIMARY RECEPTOR FOR SOME HIV-2 ISOLATES AND AS A CO-RECEPTOR WITH CD4 FOR HIV-1 X4 VIRUSES (LYMPHOCYTE-TROPIC HIV-1 VIRUSES, ALSO CALLED SYNCYTIUM-INDUCING (SI) STRAINS). PROMOTES ENV-MEDIATED FUSION OF THE VIRUS.
- **SUBCELLULAR LOCATION:** Integral membrane protein.
- **ALTERNATIVE PRODUCTS:** At least 2 isoforms; 1 (shown here) and 2/CXCR4-LO; are produced by alternative splicing. Isoform 2 has been shown to exist only in human so far.
- **TISSUE SPECIFICITY:** Expressed in numerous tissues, such as peripheral blood leukocytes, spleen, thymus, spinal cord, heart, placenta, lung, liver, skeletal muscle, kidney, pancreas, cerebellum, cerebral cortex and medulla (in microglia as well as in astrocytes), brain microvascular, coronary artery and umbilical cord endothelial cells. Isoform 1

is predominant in all tissues tested.

- **PTM:** SULFATED.
- **SIMILARITY:** BELONGS TO FAMILY 1 OF G-PROTEIN COUPLED RECEPTORS.
- **CAUTION:** WAS ORIGINALLY (REF.1 AND REF.2) THOUGHT TO BE A RECEPTOR FOR NEUROPEPTIDE Y, TYPE 3 (NPY3-R).
- **DATABASE:** NAME=PROW; NOTE=PROW 2:50-58(2001);
WWW="http://www.ncbi.nlm.nih.gov/prow/guide/192999234_g.htm".

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Cross-references


EMBL	L01639; AAA16594.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	M99293; AAA16617.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	X71635; CAA50641.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	L06797; AAA03209.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	D10924; BAA01722.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF005058; AAB93982.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF052572; AAC34581.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AF025375; AAB81970.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	Y14739; CAA75034.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	AJ224869; CAA12166.1; ALT_SEQ. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	AF147204; AAF00130.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
	U89798; AAC03718.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
Genew	S32761; S32761.
CleanEx	A45747; A45747.
MIM	HGNC:2561; CXCR4.
GeneCards	HGNC:2561; CXCR4.
GeneLynx	162643 [NCBI / EBI] .
SOURCE	CXCR4.
Ensembl	CXCR4; Homo sapiens.
InterPro	P30991; Homo sapiens. [Entry / Contig view]
Pfam	IPR000276; GPCR_Rhodpsn.
PRINTS	Graphical view of domain structure.
PROSITE	PF00001; 7tm_1; 1.
GPCRDB	PR00237; GPCRRHODOPSN.
GPCRDB-Snakes	PS00237; G_PROTEIN_RECEP_F1_1; 1.
ProDom	PS50262; G_PROTEIN_RECEP_F1_2; 1.
BLOCKS	P30991; CCR4_HUMAN.
ProtoNet	P30991.
ProtoMap	P30991.
PRESAGE	P30991.
DIP	P30991.
ModBase	P30991.
SWISS-2DPAGE	P30991.
	Get region on 2D PAGE.


Keywords

G-protein coupled receptor; Transmembrane; Glycoprotein; Sulfation; Antigen; Alternative splicing.

Features

Key	From	To	Length	Description
DOMAIN	1	39	39	EXTRACELLULAR (POTENTIAL) .
TRANSMEM	40	63	24	1 (POTENTIAL) .
DOMAIN	64	79	16	CYTOPLASMIC (POTENTIAL) .
TRANSMEM	80	99	20	2 (POTENTIAL) .
DOMAIN	100	110	11	EXTRACELLULAR (POTENTIAL) .
TRANSMEM	111	132	22	3 (POTENTIAL) .
DOMAIN	133	154	22	CYTOPLASMIC (POTENTIAL) .
TRANSMEM	155	175	21	4 (POTENTIAL) .
DOMAIN	176	200	25	EXTRACELLULAR (POTENTIAL) .
TRANSMEM	201	220	20	5 (POTENTIAL) .
DOMAIN	221	240	20	CYTOPLASMIC (POTENTIAL) .
TRANSMEM	241	261	21	6 (POTENTIAL) .
DOMAIN	262	285	24	EXTRACELLULAR (POTENTIAL) .
TRANSMEM	286	305	20	7 (POTENTIAL) .
DOMAIN	306	352	47	CYTOPLASMIC (POTENTIAL) .
MOD_RES	21	21		SULFATION (POTENTIAL) .
CARBOHYD	11	11		N-LINKED (GLCNAC...) (POTENTIAL) .
DISULFID	109	186		BY SIMILARITY.
VARSP LIC	1	5		MEGIS -> MSIPLPLLQ (IN ISOFORM 2) .

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Sequence information

Length: 352 AA

Molecular weight: 39745 Da

CRC64: 8C8476A186786B83 [This is a checksum on the sequence]

10	20	30	40	50	60
MEGISIYTS	DNYTEEMGS	GDYDSMKEPC	FR EENANFNK	IFLPTIYSIIF	L TGIVGNGL
70	80	90	100	110	120
LVMGYQKK	RLRSMTDKY	RLSVADLLF	VITLPFWAVD	AVANWYFGN	FLCK AVHVI
130	140	150	160	170	180
YSSVLILA	FI SLDRYLA	IVHATNSQR	PRKL LAEKV	VYVGWIPALL	LLTIP DFIFA
190	200	210	220	230	240
DDRYICDR	FY PNDLVV	VVFQ FQHIM	VGLIL PGIV	ILSCYC IISK	LSHSK GHQ
250	260	270	280	290	300
TVILILAF	FA CWLPHY	YIGIS IDSF	ILLEII KQGC	EFENTV HKW	ISITEAL
310	320	330	340	350	
LYAFLGAK	FK TSAQHA	LTSTV SRGS	SLKILS KGK	RGGHSSV	STESSESS
					SS

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